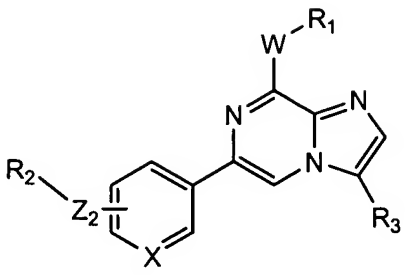
CLAIMS

What is claimed is:

1. A compound having Formula 1:



(Formula 1)

and the pharmaceutically-acceptable salts and prodrugs thereof, wherein:

$R_1$ is pyridyl or pyrimidinyl, each of which is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, $C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, $C_3$-$C_7$cycloalkyl, $C_1$-$C_6$alkoxy, $C_1$-$C_6$haloalkyl, $C_1$-$C_6$haloalkoxy, $C_1$-$C_6$alkylthio, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkyl, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkoxy, mono- and di-($C_1$-$C_6$alkyl)amino, amino($C_1$-$C_6$alkyl), mono- and di-($C_1$-$C_6$alkyl)amino($C_1$-$C_6$alkyl), $C_2$-$C_6$alkanoyl, and –C(O)$R_{13}$ where $R_{13}$ is $C_1$-$C_3$haloalkyl, phenyl, heterocycloalkyl, or heteroaryl;

W is phenyl or a 5- or 6-membered heteroaryl containing from 1 to 4 heteroatoms independently chosen from nitrogen, oxygen, and sulfur; wherein W is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, oxo, $C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, $C_3$-$C_7$cycloalkyl, $C_1$-$C_6$alkoxy, $C_1$-$C_6$haloalkyl, $C_1$-$C_6$haloalkoxy, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkyl, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkoxy, $C_1$-$C_6$alkylthio, mono- and di-($C_1$-$C_6$alkyl)amino, amino($C_1$-$C_6$alkyl), mono- and di-($C_1$-$C_6$alkyl)amino($C_1$-$C_6$alkyl), and $C_2$-$C_6$alkanoyl;

X is N or CH;

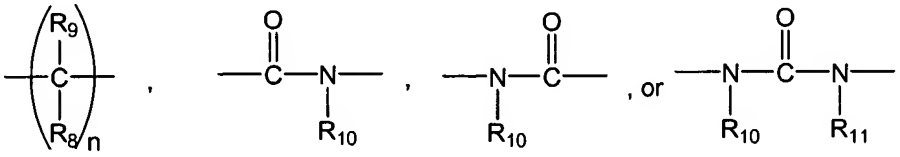
$R_2$ is $C_1$-$C_7$alkyl, $C_3$-$C_7$cycloalkyl($C_0$-$C_2$alkyl), heterocycloalkyl($C_0$-$C_2$alkyl), $C_1$-$C_6$alkoxy, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkyl, or ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkoxy; or

$R_2$ is phenyl($C_0$-$C_2$alkyl) or heteroaryl($C_0$-$C_2$alkyl), each of which is substituted with 0 to 3 substituents independently chosen from

(i) hydroxy, halogen, nitro, cyano, amino, sulfonamide, -CHO, $C_1$-$C_6$haloalkyl, and $C_1$-$C_6$haloalkoxy,and

(ii) $C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, $C_3$-$C_7$cycloalkyl, $C_1$-$C_6$alkoxy, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkyl, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkoxy, $C_1$-$C_6$alkylthio, mono- and di-($C_1$-$C_6$alkyl)amino, amino($C_1$-$C_6$alkyl), mono- and di-($C_1$-$C_6$alkyl)amino($C_1$-$C_6$alkyl), $C_2$-$C_6$alkanoyl, heterocycloalkyl($C_0$-$C_2$alkyl), and $-C(O)R_{13}$; each of which (ii) is substituted with 0 to 3 substituents independently chosen from halogen, hydroxy, amino, nitro, cyano, $C_1$-$C_4$alkoxy, $C_3$-$C_7$cycloalkyl, and mono- and di-($C_1$-$C_4$alkyl)amino;

$Z_2$ is



wherein

$R_8$ and $R_9$ are independently hydrogen, $C_1$-$C_6$alkyl, $C_1$-$C_6$alkoxy, or halogen; and n is 0, 1, or 2;

$R_{10}$ and $R_{11}$ are independently

(iii) hydrogen or $C_1$-$C_6$alkyl; or

(iv) phenyl or heteroaryl, each of which is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, $C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, $C_3$-$C_7$cycloalkyl, $C_1$-$C_6$alkoxy, $C_1$-$C_6$haloalkyl, $C_1$-$C_6$haloalkoxy, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkyl, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkoxy, $C_1$-$C_6$alkylthio, mono- and di-($C_1$-$C_6$alkyl)amino, amino($C_1$-$C_6$alkyl), mono- and di-($C_1$-$C_6$alkyl)amino($C_1$-$C_6$alkyl), $C_2$-$C_6$alkanoyl, and $-C(O)R_{13}$;

$R_3$ is hydrogen or $C_1$-$C_6$alkyl, or

$R_3$ is $C_3$-$C_7$cycloalkyl($C_0$-$C_2$alkyl), heterocycloalkyl($C_0$-$C_2$alkyl), phenyl, or heteroaryl, each of which is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, $C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, $C_3$-$C_7$cycloalkyl, $C_1$-$C_6$alkoxy, $C_1$-$C_6$haloalkyl, $C_1$-$C_6$haloalkoxy, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkyl, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkoxy, $C_1$-$C_6$alkylthio, mono- and di-($C_1$-$C_6$alkyl)amino, amino($C_1$-$C_6$ alkyl), mono- and di-($C_1$-$C_6$alkyl)amino($C_1$-$C_6$alkyl), $C_2$-$C_6$alkanoyl, and $-C(O)R_{13}$; or

$R_3$ is phenoxy phenyl, each of which phenyl rings is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, $C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, $C_3$-$C_7$cycloalkyl, $C_1$-$C_6$alkoxy, $C_1$-$C_6$haloalkyl, $C_1$-$C_6$haloalkoxy, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkyl, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkoxy, $C_1$-$C_6$alkylthio, mono- and di-($C_1$-$C_6$alkyl)amino, amino($C_1$-$C_6$alkyl), mono- and di-($C_1$-$C_6$alkyl)amino($C_1$-$C_6$alkyl), $C_2$-$C_6$alkanoyl, and $-C(O)R_{13}$.

2. A compound or salt according to Claim 1, wherein

$R_1$ is 3- or 4-pyridyl, each of which is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, $C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, $C_3$-$C_7$cycloalkyl, $C_1$-$C_6$alkoxy, $C_1$-$C_6$haloalkyl, $C_1$-$C_6$haloalkoxy, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkyl, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkoxy, $C_1$-$C_6$alkylthio, mono- and di-($C_1$-$C_6$alkyl)amino, amino($C_1$-$C_6$alkyl), mono- and di-($C_1$-$C_6$alkyl)amino($C_1$-$C_6$alkyl), and $C_2$-$C_6$alkanoyl;

W is phenyl or a 5- or 6-membered heteroaryl ring; substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, oxo, $C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, $C_3$-$C_7$cycloalkyl, $C_1$-$C_6$alkoxy, $C_1$-$C_6$haloalkyl, $C_1$-$C_6$haloalkoxy, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkyl, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkoxy, $C_1$-$C_6$alkylthio, mono- and di-($C_1$-$C_6$alkyl)amino, amino($C_1$-$C_6$alkyl), mono- and di-($C_1$-$C_6$alkyl)amino($C_1$-$C_6$alkyl), and $C_2$-$C_6$alkanoyl;

X is N or CH;

$R_2$ is $C_1$-$C_7$alkyl, $C_3$-$C_7$cycloalkyl($C_0$-$C_2$alkyl), heterocycloalkyl($C_0$-$C_2$alkyl), $C_1$-$C_6$alkoxy, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkyl, or ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkoxy; or

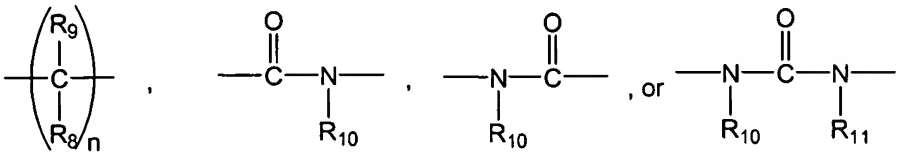
$R_2$ is phenyl($C_0$-$C_2$alkyl) or 5- or 6-membered heteroaryl($C_0$-$C_2$alkyl), each of which is substituted with 0 to 3 substituents independently chosen from

(i) hydroxy, halogen, nitro, cyano, amino, sulfonamide, -CHO, $C_1$-$C_6$haloalkyl, and $C_1$-$C_6$haloalkoxy, and

(ii) $C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, $C_3$-$C_7$cycloalkyl, $C_1$-$C_6$alkoxy, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkyl, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkoxy, $C_1$-$C_6$alkylthio, mono- and di-($C_1$-$C_6$alkyl)amino, amino($C_1$-$C_6$alkyl), mono- and di-($C_1$-$C_6$alkyl)amino($C_1$-$C_6$alkyl), $C_2$-$C_6$alkanoyl, and heterocycloalkyl($C_0$-$C_2$alkyl); each of which (ii) is substituted with 0 to 3

substituents independently chosen from halogen, hydroxy, amino, nitro, cyano, $C_1$-$C_4$alkoxy, $C_3$-$C_7$cycloalkyl, and mono- and di-($C_1$-$C_4$alkyl)amino;

$Z_2$ is



wherein

$R_8$ and $R_9$ are independently hydrogen, $C_1$-$C_6$alkyl, $C_1$-$C_6$alkoxy, or halogen; and n is 0, 1, or 2;

$R_{10}$ and $R_{11}$ are independently

(iii) hydrogen or $C_1$-$C_6$alkyl; or

(iv) phenyl or a 5- or 6 membered heteroaryl ring, each of which is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, $C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, $C_3$-$C_7$cycloalkyl, $C_1$-$C_6$alkoxy, $C_1$-$C_6$haloalkyl, $C_1$-$C_6$haloalkoxy, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkyl, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkoxy, $C_1$-$C_6$alkylthio, mono- and di-($C_1$-$C_6$alkyl)amino, amino($C_1$-$C_6$alkyl), mono- and di-($C_1$-$C_6$alkyl)amino($C_1$-$C_6$alkyl), and $C_2$-$C_6$alkanoyl;

$R_3$ is hydrogen or $C_1$-$C_6$alkyl, or

$R_3$ is $C_3$-$C_7$cycloalkyl($C_0$-$C_2$alkyl), heterocycloalkyl($C_0$-$C_2$alkyl), phenyl, or a 5- or 6-membered heteroaryl, each of which is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, $C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, $C_3$-$C_7$cycloalkyl, $C_1$-$C_6$alkoxy, $C_1$-$C_6$haloalkyl, $C_1$-$C_6$haloalkoxy, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkyl, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkoxy, $C_1$-$C_6$alkylthio, mono- and di-($C_1$-$C_6$alkyl)amino, amino($C_1$-$C_6$alkyl), mono- and di-($C_1$-$C_6$alkyl)amino($C_1$-$C_6$alkyl), and $C_2$-$C_6$alkanoyl; or

$R_3$ is phenoxyphenyl, each of which phenyl rings is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, $C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, $C_3$-$C_7$cycloalkyl, $C_1$-$C_6$alkoxy, $C_1$-$C_6$haloalkyl, $C_1$-$C_6$haloalkoxy, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkyl, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkoxy, $C_1$-$C_6$alkylthio,

mono- and di-($C_1$-$C_6$alkyl)amino, amino($C_1$-$C_6$alkyl), mono- and di-($C_1$-$C_6$alkyl)amino($C_1$-$C_6$alkyl), and $C_2$-$C_6$alkanoyl.

3. A compound or salt according to Claim 2 wherein

$R_1$ is 3-pyridyl or 4-pyridyl, each of which is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, halogen, $C_1$-$C_6$alkyl, $C_3$-$C_7$cycloalkyl, $C_1$-$C_6$alkoxy, $C_1$-$C_2$haloalkyl, $C_1$-$C_2$haloalkoxy, and mono- and di-($C_1$-$C_4$alkyl)amino.

4. A compound or salt according to Claim 3 wherein

$R_1$ is 3-pyridyl or 4-pyridyl, each of which is substituted with 0 to 2 substituents independently chosen from fluoro, chloro, bromo, $C_1$-$C_2$alkyl, and $C_1$-$C_2$alkoxy.

5. A compound or salt according to any one of Claims 1 to 4 wherein

W is phenyl, pyridyl, pyrimidinyl, imidazolyl, pyrrolyl, pyrazolyl, furanyl, thienyl, oxazolyl, or isoxazolyl, each of which is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, oxo, $C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, $C_3$-$C_7$cycloalkyl, $C_1$-$C_6$alkoxy, $C_1$-$C_6$haloalkyl, $C_1$-$C_6$haloalkoxy, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkyl, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkoxy, $C_1$-$C_6$alkylthio, mono- and di-($C_1$-$C_6$alkyl)amino, amino($C_1$-$C_6$alkyl), mono- and di-($C_1$-$C_6$alkyl)amino($C_1$-$C_6$alkyl), and $C_2$-$C_6$alkanoyl

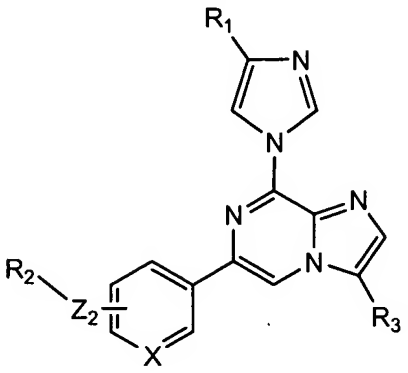
6. A compound or salt according to Claim 5 wherein

W is phenyl, pyridyl, pyrimidinyl, imidazolyl, pyrrolyl, pyrazolyl, furanyl, thienyl, oxazolyl, or isoxazolyl, each of which is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, halogen, oxo, $C_1$-$C_4$alkyl, $C_1$-$C_4$alkoxy, $C_1$-$C_2$haloalkyl, $C_1$-$C_2$haloalkoxy, and mono- and di-($C_1$-$C_4$alkyl)amino.

7. A compound or salt according to Claim 6, wherein

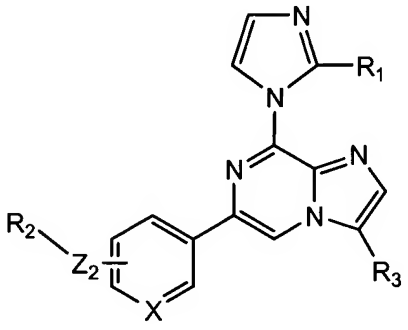
W is imidazolyl, pyrrolyl, or pyrazolyl, each of which is substituted with 0 to 2 substituents independently chosen from hydroxy, cyano, halogen, oxo, $C_1$-$C_4$alkyl, $C_1$-$C_4$alkoxy, trifluoromethyl, and trifluoromethoxy.

8. A compound or salt according to any one of Claims 1 to 4 of Formula 2



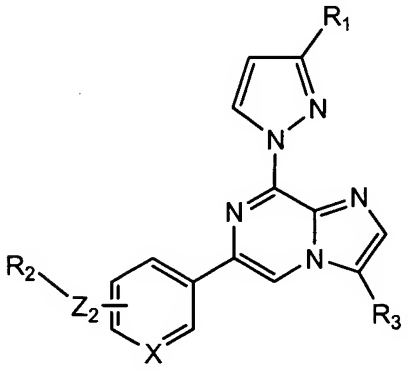
(Formula 2).

9. A compound or salt according to any one of Claims 1 to 4 of Formula 3



(Formula 3).

10. A compound or salt according to any one of Claims 1 to 4 of Formula 4

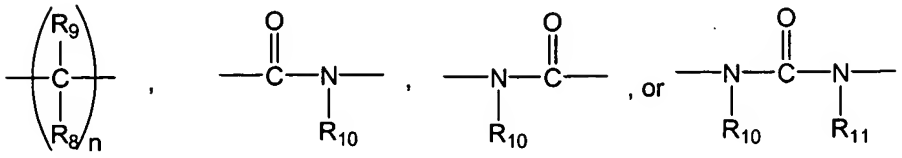


(Formula 4).

11. A compound or salt according to any one of Claims 1 to 10, wherein X is N.

12. A compound or salt according to any one of Claims 1 to 10, wherein X is CH.

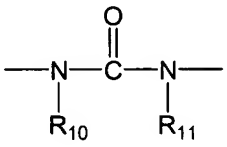
13. A compound or salt according to any one of Claims 1 to 12 wherein $Z_2$ is



wherein

$R_8$ and $R_9$ are independently hydrogen or $C_1$-$C_6$alkyl; and n is 0, 1, or 2; and $R_{10}$ and $R_{11}$ are independently hydrogen, $C_1$-$C_6$alkyl, or phenyl.

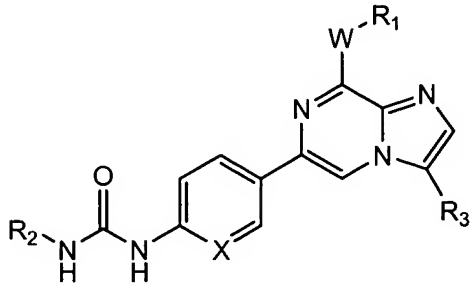
14. A compound or salt according to Claim 13, wherein $Z_2$ is



wherein, $R_{10}$ and $R_{11}$ are independently hydrogen, methyl or ethyl.

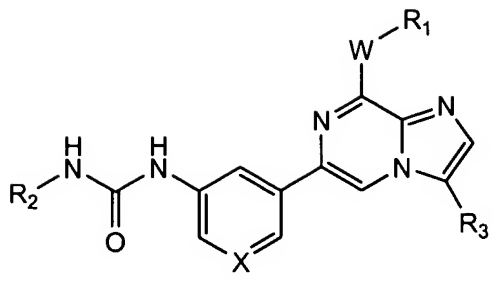
15. A compound or salt according to Claim 14 wherein $R_{10}$ and $R_{11}$ are both hydrogen.

16. A compound or salt according to any one of Claims 1 to 15 of Formula 5



(Formula 5).

17. A compound or salt according to any one of Claims 1 to 15 of Formula 6



(Formula 6).

18. A compound or salt according to any one of Claims 1 to 17 wherein

$R_2$ is phenyl, pyridyl, pyrimidinyl, pyrazinyl, imidazolyl, pyrrolyl, furanyl, thienyl, oxazolyl, or isoxazolyl, each of which may be either directly attached or bound via a $C_1$-$C_2$alkyl linker, and each of which is substituted with 0 to 3 substituents independently chosen from:

(i) hydroxy, halogen, nitro, cyano, amino, sulfonamide, -CHO, $C_1$-$C_6$haloalkyl, and $C_1$-$C_6$haloalkoxy, and

(ii) $C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, $C_3$-$C_7$cycloalkyl, $C_1$-$C_6$alkoxy, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkyl, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkoxy, $C_1$-$C_6$alkylthio, mono- and di-($C_1$-$C_6$alkyl)amino, amino($C_1$-$C_6$alkyl), mono- and di-($C_1$-$C_6$alkyl)amino($C_1$-$C_6$alkyl), $C_2$-$C_6$alkanoyl, and heterocycloalkyl($C_0$-$C_2$alkyl); each of which (ii) is substituted with 0 to 3 substituents independently chosen from halogen, hydroxy, amino, nitro, cyano, $C_1$-$C_4$alkoxy, $C_3$-$C_7$cycloalkyl, and mono- and di-($C_1$-$C_4$alkyl)amino.

19. A compound or salt according to Claim 18, wherein

$R_2$ is phenyl($C_0$-$C_2$alkyl), pyridyl($C_0$-$C_2$alkyl), or pyrimidinyl($C_0$-$C_2$alkyl), each of which is substituted with 0 to 3 substituents independently chosen from:

(i) hydroxy, halogen, nitro, cyano, amino, $C_1$-$C_2$haloalkyl, and $C_1$-$C_2$haloalkoxy, and

(ii) $C_1$-$C_6$alkyl, $C_3$-$C_7$cycloalkyl, $C_1$-$C_6$alkoxy, ($C_1$-$C_6$alkoxy)$C_1$-$C_6$alkyl, $C_1$-$C_4$alkylthio, mono- and di-($C_1$-$C_4$alkyl)amino, mono- and di-($C_1$-$C_4$alkyl)amino($C_1$-$C_4$alkyl), and heterocycloalkyl($C_0$-$C_2$alkyl); each of which (ii) is substituted with 0 to 3 substituents independently chosen from halogen, hydroxy, amino, nitro, cyano, $C_1$-$C_4$alkoxy, $C_3$-$C_7$cycloalkyl, and mono- and di-($C_1$-$C_4$alkyl)amino.

20. A compound or salt according to Claim 19, wherein

$R_2$ is phenyl or benzyl, each of which is substituted with 0 to 3 substituents independently chosen from halogen, hydroxy, amino, $C_1$-$C_4$alkyl, $C_1$-$C_4$alkoxy, $C_1$-$C_4$alkylthio, $C_1$-$C_2$haloalkyl, and $C_1$-$C_2$haloalkoxy.

21. A compound or salt according to any one of Claims 1 to 20, wherein

$R_3$ is hydrogen or $C_1$-$C_6$alkyl, or

$R_3$ is $C_3$-$C_7$cycloalkyl, ($C_3$-$C_7$cycloalkyl)methyl, heterocycloalkyl, (heterocycloalkyl)$C_1$-$C_2$alkyl, phenyl, phenyl, pyridyl, pyrimidinyl, pyrazinyl, imidazolyl, pyrrolyl, furanyl, thienyl, oxazolyl, or isoxazolyl, each of which is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, halogen, $C_1$-$C_6$alkyl, $C_3$-$C_7$cycloalkyl, $C_1$-$C_6$alkoxy, $C_1$-$C_2$haloalkyl, $C_1$-$C_2$haloalkoxy, and mono- and di-($C_1$-$C_4$alkyl)amino; or

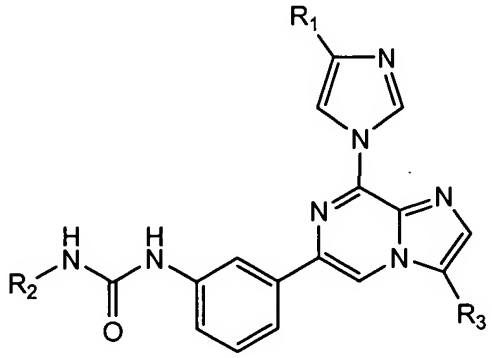
$R_3$ is phenoxyphenyl, each of which phenyl rings is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, halogen, $C_1$-$C_6$alkyl, $C_3$-$C_7$cycloalkyl, $C_1$-$C_6$alkoxy, $C_1$-$C_2$haloalkyl, $C_1$-$C_2$haloalkoxy, and mono- and di-($C_1$-$C_4$alkyl)amino.

22. A compound or salt according to Claim 21, wherein

$R_3$ is hydrogen, $C_1$-$C_6$alkyl, $C_3$-$C_7$cycloalkyl($C_0$-$C_1$alkyl), phenyl, or phenoxyphenyl.

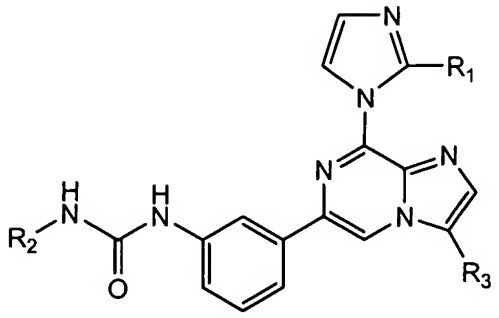
23 A compound or salt according to Claim 22, wherein $R_3$ is hydrogen or $C_1$-$C_4$alkyl.

24. A compound or salt according to Claim 1 of Formula 7



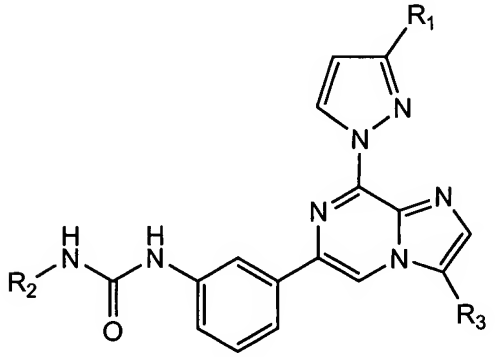

(Formula 7).

25. A compound or salt according to Claim 1 of Formula 8



(Formula 8).

26. A compound or salt according to Claim 1 of Formula 9



(Formula 9).

27. A compound or salt according to any one of Claims 24 to 26, wherein

$R_1$ is 3-pyridyl or 4-pyridyl, each of which is substituted with 0 to 2 substituents independently chosen from fluoro, chloro, bromo, $C_1$-$C_2$alkyl, and $C_1$-$C_2$alkoxy;

$R_2$ is phenyl or benzyl, each of which is substituted with 0 to 3 substituents independently chosen from: (i) hydroxy, halogen, amino, $C_1$-$C_2$haloalkyl, and $C_1$-$C_2$haloalkoxy, and

(ii) $C_1$-$C_6$alkyl, $C_1$-$C_6$alkoxy, mono- and di-($C_1$-$C_4$alkyl)amino, mono- and di-($C_1$-$C_4$alkyl)amino($C_1$-$C_4$alkyl), piperazinyl($C_0$-$C_1$alkyl), piperidinyl($C_0$-$C_1$alkyl) and morpholinyl($C_0$-$C_1$alkyl); each of which (ii) is substituted with 0 to 3 substituents independently chosen from halogen, hydroxy, amino, $C_1$-$C_2$alkoxy, and mono- and di-($C_1$-$C_4$alkyl)amino; and

$R_3$ is hydrogen or $C_1$-$C_4$alkyl.

28. A compound or form thereof according to Claim 1, wherein the compound is:

1-(2-Methoxy-5-trifluoromethyl-phenyl)-3-{3-[8-(2-pyridin-4-yl-imidazol-1-yl)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-urea;

1-(4-Methoxy-3-trifluoromethyl-phenyl)-3-{3-[8-(2-pyridin-4-yl-imidazol-1-yl)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-urea;

1-(2-Methoxy-5-trifluoromethyl-phenyl)-3-{3-[8-(2-pyridin-3-yl-imidazol-1-yl)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-urea;

1-(5-Chloro-2-methoxy-phenyl)-3-{3-[8-(2-pyridin-4-yl-imidazol-1-yl)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-urea;

1-(5-Fluoro-2-trifluoromethyl-phenyl)-3-{3-[8-(2-pyridin-4-yl-imidazol-1-yl)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-urea;

1-(5-Chloro-2-trifluoromethyl-phenyl)-3-{3-[8-(2-pyridin-4-yl-imidazol-1-yl)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-urea;

1-(5-Chloro-2,4-dimethoxy-phenyl)-3-{3-[8-(2-pyridin-4-yl-imidazol-1-yl)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-urea;

1-(4-Methyl-3-trifluoromethyl-phenyl)-3-{3-[8-(2-pyridin-4-yl-imidazol-1-yl)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-urea;

1-(4-Chloro-3-trifluoromethyl-phenyl)-3-{3-[8-(2-pyridin-4-yl-imidazol-1-yl)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-urea; or

1-(2-Methoxy-5-trifluoromethyl-phenyl)-3-{3-[8-(3-pyridin-4-yl-pyrazol-1-yl)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-urea.

29. A compound or form thereof according to any one of Claims 1 to 28, wherein the compound exhibits a $IC_{50}$ of 1 micromolar or less in a standard in *vitro* assay of $EphB_4$ kinase activity.

30. A compound or form thereof according to any one of Claims 1 to 28, wherein the compound exhibits a $IC_{50}$ of 500 nanomolar or less in a standard in *vitro* assay of $EphB_4$ kinase activity.

31. A compound or form thereof according to any one of Claims 1 to 28, wherein the compound exhibits a $IC_{50}$ of 100 nanomolar or less in a standard in *vitro* assay of $EphB_4$ kinase activity.

32. A pharmaceutical composition, comprising a compound or form thereof according to any one of Claims 1 to 31, together with at least one pharmaceutically acceptable carrier or excipient.

33. A pharmaceutical composition according to Claim 32, wherein the composition is formulated as an injectable fluid, an aerosol, a cream, a gel, a tablet, a pill, a capsule, a syrup, ophthalmic solution, or a transdermal patch.

34. A packaged pharmaceutical composition, comprising

(a) a pharmaceutical composition according to Claim 32 in a container; and

(b) instructions for using the composition to treat a patient suffering from an disease or disorder responsive to kinase activity modulation of one or more tyrosine kinase.

35. The packaged pharmaceutical composition of Claim 34 wherein the disease or disorder responsive to kinase activity modulation is cancer or a disease characterized by pathological angiogenesis.

36. The package pharmaceutical composition of Claim 34 wherein the disease characterized by pathological angiogenesis is a cancerous tumor, macular degeneration, or diabetic retinopathy.

37. A method of reducing medication error and enhancing therapeutic compliance of a patient being treated for a disease or disorder responsive to tyrosine kinase activity modulation, the method comprising providing a packaged pharmaceutical preparation according to Claim 34 wherein the instructions additionally include contraindication and adverse reaction information pertaining to the package pharmaceutical composition.

38. A method of modulating $EphB_4$ kinase activity, the method comprising contacting cells expressing $EphB_4$ kinase with a compound or form thereof according to any one of Claims 1 to 28 in an amount sufficient to detectably inhibit $EphB_4$ kinase activity *in vitro*.

39. A method of modulating VEGF-R2 activity, the method comprising contacting cells expressing VEGF-R2 with a compound or form thereof according to any one of Claims 1 to 28 in an amount sufficient to detectably inhibit VEGF-R2 activity *in vitro*.

40. A method of modulating c-Kit activity, the method comprising contacting cells expressing c-Kit with a compound or form thereof according to any one of Claims 1 to 28 in an amount sufficient to detectably inhibit c-Kit activity *in vitro*.

41. A method of modulating Tie-2 activity, the method comprising contacting cells expressing Tie-2 with a compound or form thereof according to any one of Claims 1 to 28 in an amount sufficient to detectably inhibit Tie-2 activity *in vitro*.

42. A method of modulating VEGF-R2, $EphB_4$, Tie-2, and c-Kit activity, the method comprising contacting cells expressing VEGF-R2, $EphB_4$, Tie-2, and c-Kit with a compound having a molecular weight less than 600 amu in an amount sufficient to detectably inhibit the activity of at least one of VEGF-R2, $EphB_4$, Tie-2, or c-Kit *in vitro*.

43. The method of Claim 42 wherein the compound is a heterocyclic compound.

44. The method of Claim 43 wherein the compound is a heterocyclic compound comprising a bicyclic heterocyclic group.

45. The method of Claim 43 wherein the compound is a compound of Claims 1 to 28 or form thereof.

46. A method of treating a patient having a disease or disorder responsive to kinase activity modulation comprising administering to the patient an effective amount of a compound according to any one of Claims 1 to 28.

47. The method of 46 wherein the patient is a human.

48. The method of Claim 46 wherein the patient is a cat or dog.

49. The method of Claim 46 wherein the disease or disorder responsive kinase activity modulation is cancer or a disease characterized by pathological angiogenesis.

50. The method of Claim 49 wherein the disease characterized by pathological angiogenesis is a cancerous tumor, macular degeneration, or diabetic retinopathy.

51. The method of Claim 46 wherein the compound or form is administered orally.

52. A method for determining the presence or absence of an angiogenic kinase in a sample comprising contacting the sample with a compound or form thereof according to any one of Claims 1 to 28 under conditions that permit binding of the compound or form to the angiogenic kinase, detecting a level of the compound or form bound to the angiogenic kinase, and therefrom determining the presence or absence of the angiogenic kinase.

53. The method of Claim 52 wherein the angiogenic kinase is Tie-2, VEGF-R2, or $EphB_4$.

54. The method of Claim 53 wherein the compound or form thereof is radiolabelled.

55. The method of Claim 53, which additionally comprises

separating unbound compound from bound compound; and determining the amount of bound compound in the sample.

56. The method of claim 42 wherein the cells expressing VEGF-R2, $EphB_4$, Tie-2, and c-Kit with a compound are contacted with the compound having a molecular weight less than 600 amu in an amount sufficient to detectably inhibit the activity of VEGF-R2, $EphB_4$, Tie-2, and c-Kit *in vitro*.